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* * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

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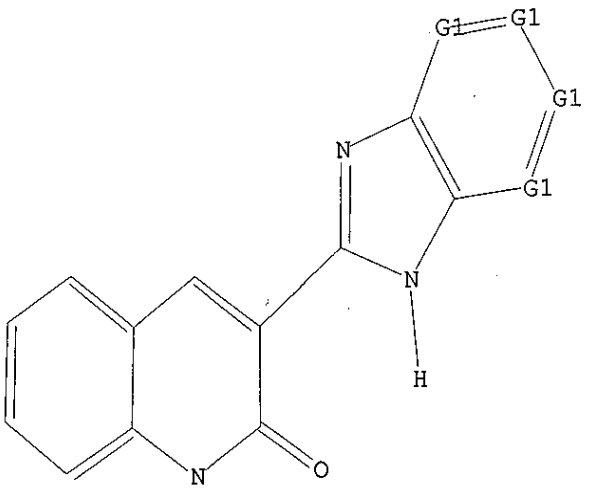


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Structure attributes must be viewed using STN Express query preparation.


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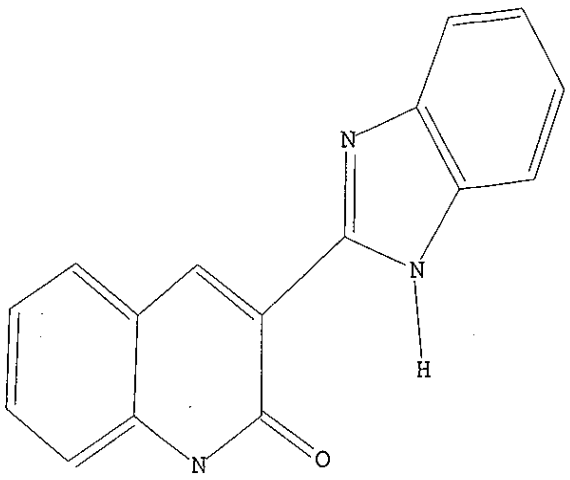

Structure attributes must be viewed using STN Express query preparation.

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L6   ANSWER 1 OF 3  CA  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         138:153534  CA
TITLE:                    Preparation of benzimidazolyl-substituted quinolinone
                          derivatives and analogs, with inhibitory action
                          against vascular endothelial growth factor receptor
                          tyrosine kinase, and useful as anticancer agents
INVENTOR(S):              Renhowe, Paul A.; Pecchi, Sabina; Machajewski, Timothy
                          D.; Shafer, Cynthia M.; Taylor, Clarke; McCrea,
                          William R.; McBride, Christopher; Jazan, Elisa
PATENT ASSIGNEE(S):       Chiron Corporation, USA
SOURCE:                   U.S. Pat. Appl. Publ., 69 pp., Cont.-in-part of U.S.
                          Pat. Appl. 2002 107,392.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
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Parent

US 2003028018	A1	20030206	US 2002-116117	20020405	
US 2002107392	A1	20020808	US 2001-951265	20010911	
US 6605617	B2	20030812			
US 2003158224	A1	20030821	US 2002-284017	20021030	
WO 2003087095	A1	20031023	WO 2003-US10463	20030404	

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-232159P P 20000911
US 2001-951265 A2 20010911
US 2002-116117 A 20020405

OTHER SOURCE(S): MARPAT 138:153534

GI

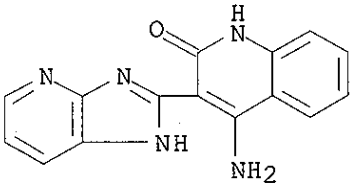
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. of formulas I and II are provided [for I: Z = O, S, (un)substituted NH; Y = certain OH derivs., CHO, esters and amides of CO2H, certain NH2 derivs.; R1-R4 = H, halo, cyano, NO2, OH or derivs., NH2 or derivs., (un)substituted amidinyl, guanidinyl, alk(en/yn)yl, aryl, heterocyclyl, CHO, CO2H and esters and amides; R5-R8 = H, halo, NO2, OH or derivs., NH2 or derivs., SH or derivs., cyano, etc.; R9 = H, OH, (un)substituted alkoxy or aryloxy, NH2 or derivs., (un)substituted alkyl or aryl, CHO, alkanoyl, aroyl; for II: A, B, D, E = C or N, with at least one being N; Y = H, OH or derivs., SH or derivs., NH2 or derivs., cyano, various acyl groups, (un)substituted alk(en/yn)yl, aralkyl, heterocycloalkyl, aryl, etc.; R1-R8 = H, halo, NO2, cyano, OH or derivs., NH2 or derivs., acyl, SH or derivs., etc.; R9 = H, OH, (un)substituted alkoxy, aryloxy, NH2 or derivs., aryl, CHO, alkanoyl, aroyl]. Also provided are pharmaceutical formulations including the compds. or their pharmaceutically acceptable salts and a pharmaceutically acceptable carrier, which may be prepd. by mixing the compds. or salts with a carrier and water. A disclosed method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient. Claims include tautomers of the compds., pharmaceutically acceptable salts, and pharmaceutically acceptable salts of the tautomers. I and II are inhibitors of receptor tyrosine kinases, and particularly of vascular endothelial growth factor receptor (VEGFR) tyrosine kinase. As such, they are inhibitors of angiogenesis, and thereby act as anticancer agents. Approx 270 invention compds. are listed, with detailed prepns. given for about 50 compds. Several general preparatory methods are discussed in detail. For instance, cyclocondensation of Et 2-(benzimidazol-2-yl)acetate with the corresponding ortho-amino nitrile (prepns. given), carried out in refluxing ClCH2CH2Cl in the presence of SnCl4, gave the invention quinolinone III. Many compds. I and II had in vitro IC50 values of less than 10 .mu.M with respect to flt-1 (VEGFR1), KDR (VEGFR2) and bFGF kinases (recombinant, expressed in Sf9 insect cells).

IT **405168-52-7P**, 4-Amino-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-

2(1H)-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)

RN 405168-52-7 CA
CN 2(1H)-Quinolinone, 4-amino-3-(1H-imidazo[4,5-b]pyridin-2-yl)- (9CI) (CA INDEX NAME)



IT **405168-52-7P**, 4-Amino-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one **405168-53-8P**, 4-Amino-3-(5-(morpholin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one **405168-54-9P**, 4-Amino-5-((2R,6S)-2,6-dimethylmorpholin-4-yl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one **405168-55-0P**, 4-Amino-3-[5-[3-(dimethylamino)pyrrolidin-1-yl]-3H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one **405169-25-7P**, 4-Amino-3-[5-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one **405169-26-8P**, 4-Amino-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one **405169-79-1P**, 4-[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-6,7-difluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one **405169-83-7P**, 6-(3-Acetylphenyl)-4-[((3R)-1-azabicyclo[2.2.2]oct-3-yl)amino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one **405169-85-9P**, 4-[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-6-fluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)-7-(morpholin-4-yl)quinolin-2(1H)-one **405169-87-1P**, N-[3-[4-[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-2-oxo-1,2-dihydroquinolin-6-yl]phenyl]acetamide **405169-89-3P**, 4-[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-6-fluoro-7-(1H-imidazol-1-yl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one **405169-92-8P**, 6-Chloro-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one **405169-96-2P**, 4-[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-(trifluoromethyl)phenyl]quinolin-2(1H)-one **405169-97-3P**, 4-[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-(methyloxy)phenyl]quinolin-2(1H)-one **405170-02-7P**, 4-[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-6-(2,4-dichlorophenyl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one **405170-06-1P**, 4-Hydroxy-3-(1H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)

L6 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 136:263158 CA
TITLE: Benzimidazolyl-substituted quinolinone derivatives and analogs, with inhibitory action against vascular

endothelial growth factor receptor tyrosine kinase, and useful as anticancer agents

INVENTOR(S): Renhowe, Paul; Pecchi, Sabina; Machajewski, Tim; Shafer, Cynthia; Taylor, Clarke; McCrea, Bill; McBride, Chris; Jazan, Elisa; Wernette-Hammond, Mary-Ellen; Harris, Alex

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: PCT Int. Appl., 207 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

Bad Date

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001093275	A5	20020326	AU 2001-93275	20010911
EP 1317442	A1	20030611	EP 2001-973722	20010911
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NO 2003001097	A	20030325	NO 2003-1097	20030310

PRIORITY APPLN. INFO.: US 2000-232159P P 20000911
WO 2001-US42131 W 20010911

OTHER SOURCE(S): MARPAT 136:263158

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

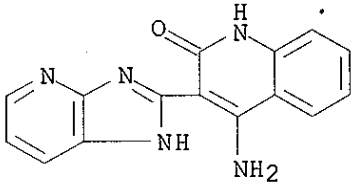
AB Title compds. of formulas I and II are provided [for I: Z = O, S, (un)substituted NH; Y = certain OH derivs., CHO, esters and amides of CO2H, certain NH2 derivs.; R1-R4 = H, halo, cyano, NO2, OH or derivs., NH2 or derivs., (un)substituted amidinyl, guanidinyl, alk(en/yn)yl, aryl, heterocyclyl, CHO, CO2H and esters and amides; R5-R8 = H, halo, NO2, OH or derivs., NH2 or derivs., SH or derivs., cyano, etc.; R9 = H, OH, (un)substituted alkoxy or aryloxy, NH2 or derivs., (un)substituted alkyl or aryl, CHO, alkanoyl, aroyl; for II: A, B, D, E = C or N, with at least one being N; Y = H, OH or derivs., SH or derivs., NH2 or derivs., cyano, various acyl groups, (un)substituted alk(en/yn)yl, aralkyl, heterocycloalkyl, aryl, etc.; R1-R8 = H, halo, NO2, cyano, OH or derivs., NH2 or derivs., acyl, SH or derivs., etc.; R9 = H, OH, (un)substituted alkoxy, aryloxy, NH2 or derivs., aryl, CHO, alkanoyl, aroyl]. Also provided are pharmaceutical formulations including the compds. or their pharmaceutically acceptable salts and a pharmaceutically acceptable carrier, which may be prepd. by mixing the compds. or salts with a carrier and water. A disclosed method of treating a patient includes administering a pharmaceutical formulation according to the invention to a

patient. Claims include tautomers of the compds., pharmaceutically acceptable salts, and pharmaceutically acceptable salts of the tautomers. I and II are inhibitors of receptor tyrosine kinases, and particularly of vascular endothelial growth factor receptor (VEGFR) tyrosine kinase. As such, they are inhibitors of angiogenesis, and thereby act as anticancer agents. Approx 270 invention compds. are listed, with detailed prepns. given for about 50 compds. Several general preparatory methods are discussed in detail. For instance, cyclocondensation of Et 2-(benzimidazol-2-yl)acetate with the corresponding ortho-amino nitrile (prepns. given), carried out in refluxing ClCH2CH2Cl in the presence of SnCl4, gave the invention quinolinone III. Many compds. I and II had in vitro IC50 values of less than 10 .mu.M with respect to flt-1 (VEGFR1), KDR (VEGFR2) and bFGF kinases (recombinant, expressed in Sf9 insect cells).

IT **405168-52-7P**, 4-Amino-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)

RN 405168-52-7 CA

CN 2(1H)-Quinolinone, 4-amino-3-(1H-imidazo[4,5-b]pyridin-2-yl)- (9CI) (CA INDEX NAME)



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yl)-6-[2-(methyloxy)phenyl]quinolin-2(1H)-one **405170-02-7P**, 4-[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-6-(2,4-dichlorophenyl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one **405170-06-1P**, 4-Hydroxy-3-(1H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 110:154319 CA
TITLE: Preparation of 6-heterocyclylcarbostyril derivatives for treatment of heart diseases
INVENTOR(S): Tamada, Shigeharu; Fujioka, Takafumi; Ogawa, Hidenori; Teramoto, Shuji; Kondo, Kazumi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 30 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63230687	A2	19880927	JP 1987-65202	19870318
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PRIORITY APPLN. INFO.: JP 1987-65202 19870318
OTHER SOURCE(S): MARPAT 110:154319
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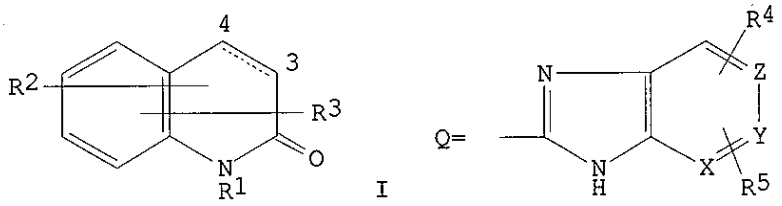


AB The title compds. [I, R1 = H, lower alkyl, lower alkenyl, phenyl-lower alkyl; R2 = Q (wherein X, Y, Z = CH or N, R4, R5 = H, lower alkoxy, halo, or NH2); R3 = H, halo, NO2, NH2, lower alkanoylamino, lower alkoxy, OH, lower alkyl, lower alkylthio, satd. 5- or 6-membered (lower alkyl) heterocyclyl, 5- or 6-membered heterocyclyl-lower alkyl; the linkage between 3- and 4-position is a single or double bond] were prepd. as cardiotonics, etc. 7-Methoxy-6-carboxy-3,4-dihydrocarbostyril 0.3 and 3,4-diaminopyridine 0.16 g were added to a 1:10 mixt. of P2O5 and Me2SO3H. The mixt. was heated 2 h at 100.degree., poured into ice-water, and made weakly alk. with 10% aq. NaOH and satd. NaHCO3. The pptd. crystals were removal by filtration, washed with H2O, dried and purified on a silica gel chromatog. to give, after acidification with HCl in EtOH, 0.29 g

7-methoxy-6-[1H-imidazo[4,5-c]pyridin-2-yl]-3,4-dihydrocarbostyril (II)-HCl.H2O. II.HCl.H2O at 300 n mol increased myocardial contractility 23.1% and coronary blood flow 0.4 mL/min in dog heart in vitro. 1 ML ampules were formulated from II 500, polyethyleneglycol 0.3, NaCl 0.9, polyoxyethylenesorbitan monooleate 0.4, sodium metabisulfite 0.1, methylparaben 0.18, propylparaben 0.02 g, and water 100 mL.

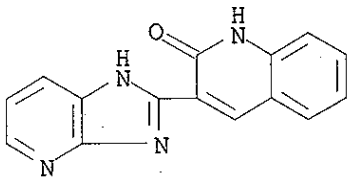
IT **119714-56-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as cardiotonic)

RN 119714-56-6 CA

CN 2(1H)-Quinolinone, 3-(1H-imidazo[4,5-b]pyridin-2-yl)-, ethanedioate (2:1) (9CI) (CA INDEX NAME)

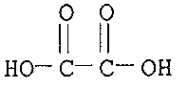
CM 1

CRN 119714-55-5
CMF C15 H10 N4 O



CM 2

CRN 144-62-7
CMF C2 H2 O4



IT **119714-56-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as cardiotonic)

=> d his

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L2 STRUCTURE UPLOADED
L3 327 S L1 FULL
L4 309 S L2 FULL
L5 18 S L3 NOT L4

FILE 'CA' ENTERED AT 13:57:15 ON 05 JAN 2004
L6 3 S L5

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 13:57:48 ON 05 JAN 2004